ProtaGene
Analytical Excellence

COMPANY BROCHURE

Analytics for Biologics: Stability Studies

OVER 20 YEARS OF EXPERIENCE

- GMP-certified
- Full analytical support
- Biopharmaceuticals / Biosimilars / Vaccines
- IgGs / ADC / Enzymes / Bispecifics
- State-of-the-art equipment
- Tailored solutions
- Cutting-edge methods
- Worldwide facilities

ProtaGene is a leading global CRO and a recognized expert for analytical services in protein science. The company is a preferred partner for the biopharmaceutical industry worldwide to benefit from the most advanced, integrated, and complete analytical services capabilities and platforms in biopharmaceutical development, from clone selection through drug approval to commercialization.

We generate best-in-class analytical data packages for our pharmaceutical partners and provide high-quality technical and regulatory support. ProtaGene directs all of its efforts towards advancing, de-risking, and accelerating all stages of biopharmaceutical and biosimilar development. Based on a proven one-point-of-contact project management strategy, we act throughout the service spectrum from subcontractor to fully involved project partner. Therefore, ProtaGene is recognized as a driving force in the biopharmaceutical development process.

More than 20 years of experience and a comprehensive spectrum of robust analytical methods ensure the highest quality for customers in the pharmaceutical, biotech, and life science industries. ProtaGene is thus an ideal partner in jointly compiling the quality target product profile and helping drug developers identify dosage form and stability expectations of a formulation.

In the development of new biological entities (NBEs), ProtaGene assists customer approaches through single-source service with full analytical support and outstanding project management, including compiling quality target product profile (QTPP). ProtaGene also helps biosimilar developers with a broad range of analytical methods to demonstrate biosimilarity.

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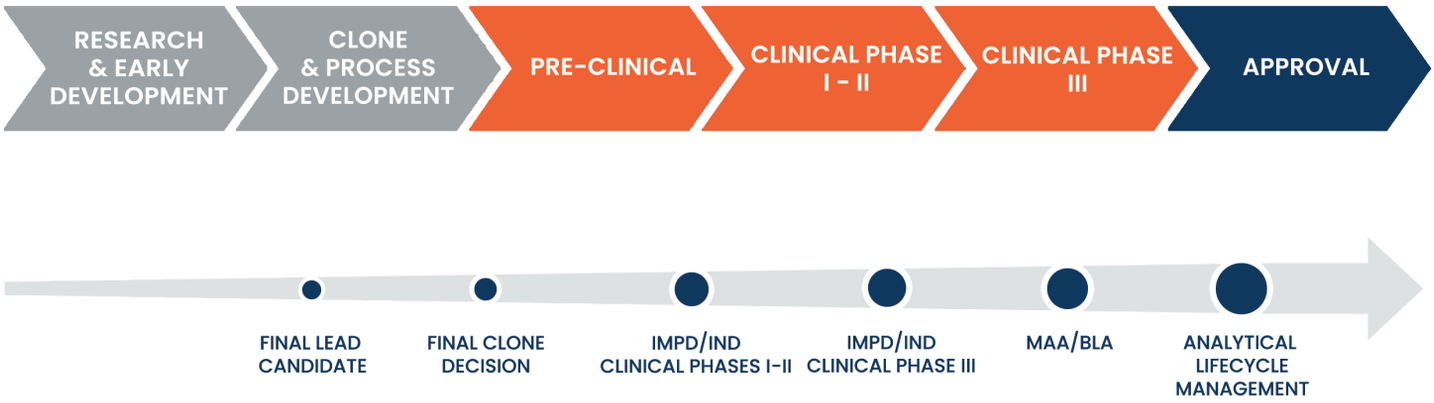

EXCELLENCE IN PROJECT MANAGEMENT

ANALYTICAL EXPERTISE FROM RESEARCH TO MARKET

REGULATORY KNOWLEDGE FOR ANALYTICAL DEVELOPMENT

Stability Studies

Stability studies are fundamental in the development of a biopharmaceutical. Proteins are sensitive to environmental factors. Changes in biopharmaceutical stability due to aggregation, degradation, chemical or physical instability can alter protein folding and structure. Consequently, this can affect the quality, safety, efficacy, and biologic activity of the molecule. Therefore, an early assessment of biopharmaceutical stability is of utmost importance.

ProtaGene offers stability programs according to the ICH guidelines Q1A(R2), Q1B, and Q5C, as well as expanded programs tailored to the client's needs. We provide scalable onsite storage capacity and in-house capabilities to evaluate the stability of pharmaceutical products. Under thoroughly qualified and controlled environmental conditions (temperature, humidity, light), various types of stability studies can be performed.

ProtaGene supports all major milestones of the analytical life cycle, from stability data for molecules in the development process to long-term stability studies for authorized market products. Our full analytical in-house capabilities not only allow for stability-indicating approaches but also various methods for extended characterization.

STORAGE CONDITIONS

- 5°C / ambient relative humidity (RH)
- 25°C / 60% RH
- 30°C / 65% RH
- 30°C / 75% RH
- 40°C / 75% RH
- Tailored conditions

STRESS CONDITIONS

- Photostability (UV and VIS)
- Freeze / thaw stress
- Agitation
- Further stress factors:
  - pH stress
  - Oxidation stress
  - Elevated temperature
  - Glycation and glycovariants

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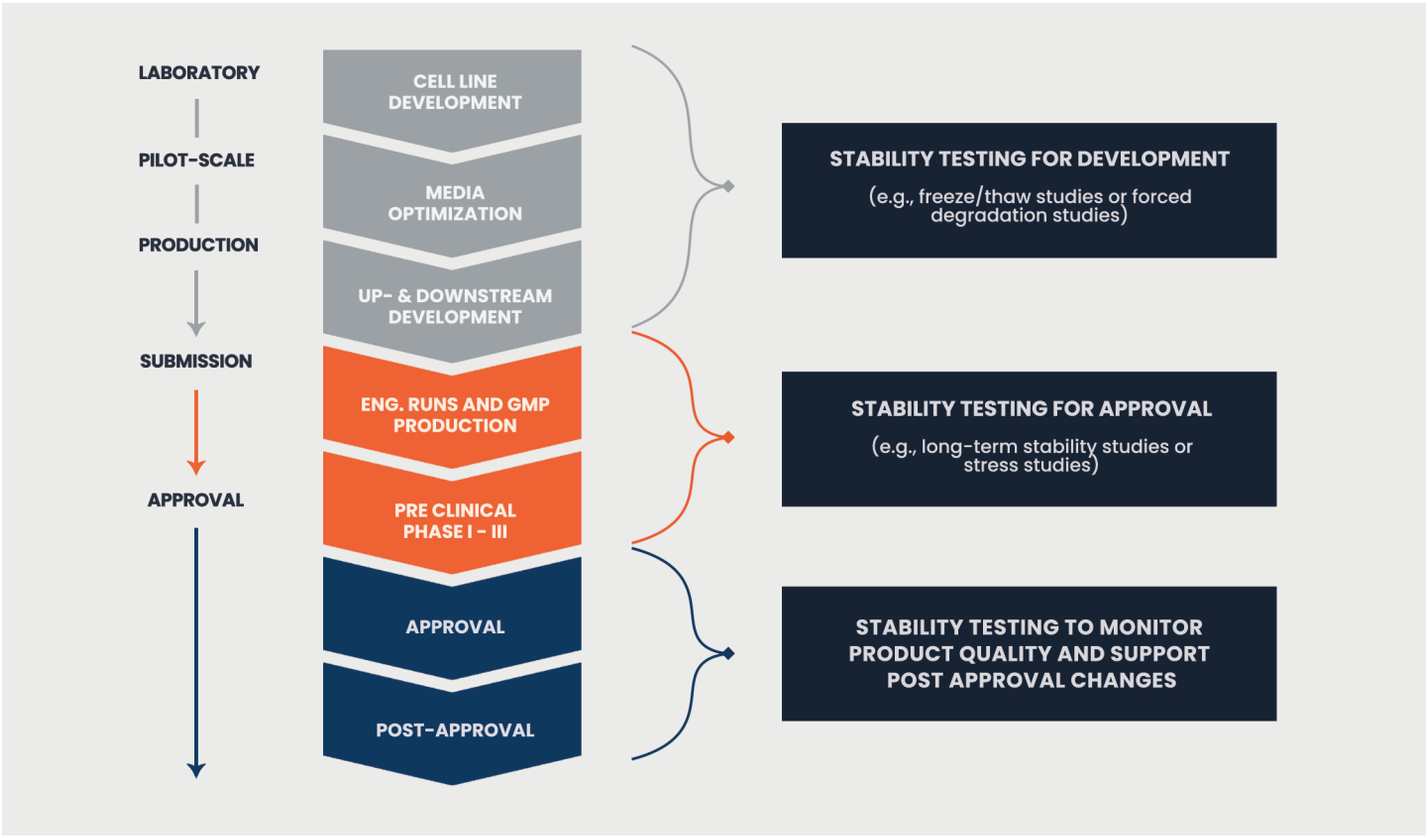

TIME POINTS / CONDITIONS	T0 (I)	T1 (1M)			T2 (3M)			T3 (6M)			T4 (9M)		T5 (12M)		T6 (18M)	T7 (24M)
	5°C	5°C	25°C	40°C	5°C	25°C	40°C	5°C	25°C	40°C	5°C	25°C	5°C	25°C	5°C	5°C
COLOR		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CLARITY	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROTEIN CONTENT BY UV	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PEPTIDE MAPPING UV	X															
CE-SDS (reduced)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CE-SDS (non-reduced)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SEC-UPLC	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CEX-UPLC	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HIC	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
BINDING ELISA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
pH VALUE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
OSMOLALITY	X									X			X	X		X
VISIBLE PARTICIES										X			X	X		X
CONTAINER CLOSURE INTEGRITY	X												X			X
EXTRACTABLE VOLUME	X															
SUB-VISIBLE PARTICLES	X	X			X			X			X		X		X	X
BACTERIAL ENDOTOXIN	X															
STERILITY	X												X			X

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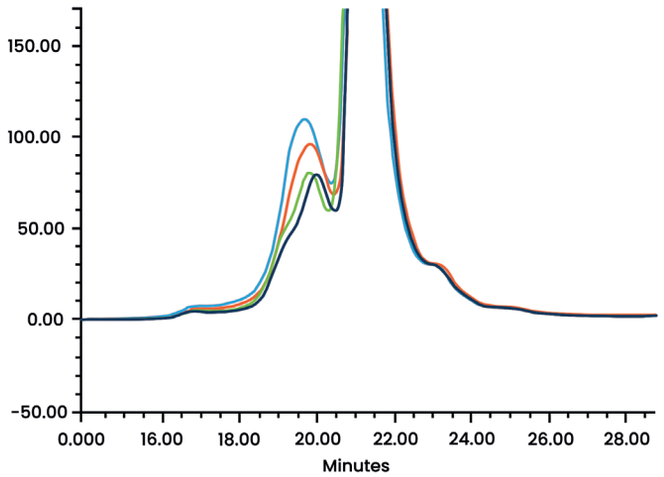
Analytical Capabilities

As stability programs are mostly conducted over several years, all analytical techniques must perform robustly to prevent out-of-specification (OOS), out-of-expectation (OOE), or out-of-trend (OOT) results that would jeopardize the study or the product release.

ProtaGene qualifies and validates all applied methods, including a comprehensive robustness assessment for critical methods, e.g., by DoE approaches. During a stability study, potential degradations/modifications can occur and have to be characterized, e.g., by mass spectrometry. The corresponding data enable the definition of critical quality attributes (CQA).

EXAMPLE CHROMATOGRAM SHOWING THE IMPACT OF STORAGE AT 40°C OVER DIFFERENT PERIODS OF TIME



PROTEIN QUANTIFICATION

- AMINO ACID ANALYSIS (AAA)
- EXTINCTION COEFFICIENT (A280)
- QUANTIFICATION BY PROTEIN-A HPLC
- ISOTOPE DILUTION MS

PROTEIN MODIFICATION

- DEAMIDATION (MS, CIEF)
- OXIDATION (MS, RP-HPLC)
- DISULFIDE LINKAGE (MS)
- FREE THIOLS (ELLMAN)
- TRUNCATIONS (CGE, MS)

AGGREGATES

- SEC-UV-MALLS
- ANALYTICAL ULTRACENTRIFUGATION (AUC)
- ASYMMETRICAL FLOW FIELD-FLOW FRACTIONATION (AF4)
- VISIBLE AND SUBVISIBLE PARTICLES (LO/MFI)

PROTEIN PRIMARY STRUCTURE

- PEPTIDE MAPPING
- INTACT MASS
- N-TERMINAL SEQUENCING (EDMAN)
- DE-NOVO SEQUENCING

PROTEIN IMPURITIES/VARIANTS

- PROCESS- & PRODUCT-RELATED IMPURITIES (IEX)
- PROTEASE ACTIVITY (FRET ASSAY)
- HCP ANALYSIS (ELISA, MS)
- HIGH-RESOLUTION 2D PAGE
- WESTERN BLOT
- RESIDUAL HOST CELL DNA (QPCR)

HIGHER ORDER STRUCTURE

- CIRCULAR DICHROISM (CD)
- INFRARED SPECTROSCOPY (FTIR)
- FLUORESCENCE SPECTROSCOPY
- DIFFERENTIAL SCANNING CALORIMETRY (DSC)
- DYNAMIC LIGHT SCATTERING (DLS)
- H-D-EXCHANGE ANALYSIS (HDX MS)

GLYCOSYLATION

- N-LINKED GLYCOSYLATION
- O-LINKED GLYCOSYLATION
- SIALIC ACID CONTENT
- MONOSACCHARIDE ANALYSIS
- GLYCOSYLATION SITE

POTENCY

- ELISA
- CELL-BASED ASSAYS
- BINDING ASSAYS

MISCELLANEOUS

- APPEARANCE, COLOR, CLARITY, TURBIDITY
- PH, OSMOLALITY, DENSITY
- POLYSORBATE QUANTIFICATION
- EXTRACTABLE VOLUME
- CONTENT UNIFORMITY OF DOSAGE UNITS

Latest mass spectrometry equipment e.g., Thermo Q-Exactive HFX

State-of-the-art industrial platform instrumentation e.g., Waters H-Class with QDA-Detector

Sophisticated analytical instrumentation e.g., Beckman Coulter AUC

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We offer stability programs according to the ICH guidelines Q1A(R2), Q1B, and Q5C, as well as expanded programs tailored to individual project needs. More than 20 years of experience in the field of GMP analytics and the comprehensive spectrum of robust analytical methods ensure the highest quality. Our analytical reports have been accepted by multiple regulatory authorities worldwide, including FDA (USA), EMA (EU), ANVISA (Brazil), and MFDS (Korea) during all stages of development.

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